Atrial Fibrillation and Heart Failure

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Virginia Commonwealth University
Two new epidemics of cardiovascular disease are emerging: **heart failure** and **atrial fibrillation**.

......heart failure ....is now responsible for more than 875,000 admissions each year in the United States.

...... the number of hospital discharges for **atrial fibrillation** more than doubled from 111,000 in 1984 to 270,000 in 1994.

# Atrial Fibrillation

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>2.2 million US; ~ 4 million in EU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>30-60 per 1000 population after age 65</td>
</tr>
<tr>
<td></td>
<td>70% of AF patients between age 65 and 85 yrs</td>
</tr>
<tr>
<td>Morbidity</td>
<td>384,000 hospitalizations (2000)</td>
</tr>
<tr>
<td></td>
<td>1-2 % of all admissions</td>
</tr>
<tr>
<td></td>
<td>12% of hospitalized patients have AF</td>
</tr>
<tr>
<td></td>
<td>15% of all strokes occur in AF patients</td>
</tr>
<tr>
<td>Mortality</td>
<td>Framingham Study reported increased total death rate (risk ratio 1.7 for men and 1.8 for women)</td>
</tr>
</tbody>
</table>

Adapted from AHA Heart and Stroke Facts Statistical Update, Podrid: AF Mechanisms and Management, 1997
Prevalence of AF in Relation to Age of Population

Adapted from Feinberg et al,3 and US Bureau of the Census6
Incidence of Atrial Fibrillation increases with Age

Murgatroyd F, Camm AJ. Atrial Arrhythmias. Lancet 1993;341:1317-1322
# Heart Failure

<table>
<thead>
<tr>
<th><strong>Prevalence</strong></th>
<th>4.7 million US; ~8-10 million in EU</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>550,000 new cases/year</td>
</tr>
<tr>
<td></td>
<td>10 per 1000 population after age 65</td>
</tr>
<tr>
<td><strong>Morbidity</strong></td>
<td>870,000 hospitalizations (1995)</td>
</tr>
<tr>
<td></td>
<td>5% to 10% of all admissions</td>
</tr>
<tr>
<td></td>
<td>Most frequent cause of hospitalizations in elderly</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>Causes or contributes to = 280,000 deaths/yr</td>
</tr>
<tr>
<td></td>
<td>Up to 60% to 70% of patients die suddenly</td>
</tr>
</tbody>
</table>

Age well-established as a principal determination of onset of heart failure

**CHF Incidences Rates (per 1,000 patients-years)**

**Age Categories**

- 45-54
- 55-64
- 65-74
- 75-84

**CHF Incidences Rates**

- Females
- Males
Atrial Fibrillation & Heart Failure

In the AFFIRM trial, 23% of patients had a history of CHF (average EF ~ 57%); in RACE trial, 50% of patients had Hx CHF;

In the major heart failure trials, 10% to 50% of patients had a diagnosis of AFIB, depending on NYHA Class.

AFFIRM Investigators, NEJM 2002; 347:1825-33
Van Gelder, NEJM 2002: 347:1834-1840
Dries D, JACC 1998: 32:695-703
Carson PE, Circulation 1993; Suppl VI: VI 102-10
Development of AF was associated with increased mortality: hazard ratio of 1.6 (95% CI, 1.2 to 2.1) in men and 2.7 (95% CI, 2.0 to 3.6) in women.

Atrial Fibrillation & Heart Failure

Complex, reciprocal relation between heart failure AF:

• Heart failure may cause AF (neurohumoral activation & atrial stretch)

• AF may promote heart failure (fast ventricular rates, irregular contractions)
Atria Fibrillation (AF) Begets Heart Failure (HF), and HF Begets AF. A Number of Mechanisms Contribute to the Initiation and Maintenance of Both AF and HF.

- Heterogeneity of Conduction
- Loss of AV Synchrony
- Altered Atrial Refractory Properties
- Rapid Ventricular Response
- Interstitial Fibrosis
- R-R Variability
- Volume and Pressure Load
- Toxicity of Therapy (eg, antiarrhythmic drugs, calcium antagonists)

Maisel, A Stevenson, L. Am. J Cardiol. 2003; 91:2D-8D
AF-Induced LV Dysfunction
Frequency: Perspective

No preexisting structural heart disease

AF
Severe LV dysfunction
Uncommon, but not rare

AF
Mild to moderate LV dysfunction
Probably common (up to 30%)

Preexisting LV dysfunction

AF
Further reduction of LV function
Clinically under recognized

## Models of Atrial Fibrillation

<table>
<thead>
<tr>
<th><strong>Reentry</strong></th>
<th><strong>Single Focus</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Multiple circuits</td>
<td>- Aconitine on RAA</td>
</tr>
<tr>
<td>- Functional reentry</td>
<td>- Focal ablation site</td>
</tr>
<tr>
<td>- Spiral waves</td>
<td>: Moe (1964)</td>
</tr>
<tr>
<td></td>
<td>: Scherf (1947)</td>
</tr>
<tr>
<td></td>
<td>: Weiss/Garfinkel (1997)</td>
</tr>
<tr>
<td></td>
<td>: Hassaguerre (1996)</td>
</tr>
</tbody>
</table>
Electrophysiological Mechanisms of Atrial Fibrillation

A

Focal Activation

LA

PV’s

ICV

SCV

RA

B

Multiple Wavelets

LA

PV’s

ICV

SCV

RA
Electrical Remodeling in Atrial Fibrillation

\[ \Delta \text{Current} \]

- $I_{Na}$
- $I_{Ca}$
- $I_f$
- $I_{TO}$
- $I_{Kuf}$
- $I_{kr}$
- $I_{KS}$
- $I_{K1}$
- $I_{KACH}$

$\downarrow 60-70\%$

$\downarrow 50-60\%$

$\downarrow 50\%$

$\uparrow$

Putative Clone

NSR

AF

20mV

100ms

SCN5a

$\alpha_{1C}$

HCN2,4

Kv4.3

Kv1.5

ERG/miRP1

KvLQT1/minK

Kir 2.1, 2.3

Kir 3.1 + Kir 3.4

Anatomical Remodelling in Atrial fibrillation

- Dedifferentiation of cardiac myocytes
- - cellular hypertrophy
- - increased fibrosis
- - increased glycogen
- - mitochondrial breakdown
- - dispersal of chromatin in nucleus
- - sarcomere distortion

Thijssen et. al, Cardiovascular Pathology 2000; 9: 17-22.
Enalapril also decreased mean AF duration from 650 to 218 seconds.

Li, D. Circulation 2001; 104:2608-14
## AF Clinical Classification

<table>
<thead>
<tr>
<th>Classification</th>
<th>Duration</th>
<th>Termination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Paroxysmal</strong></td>
<td>episodes &lt; 48 hours</td>
<td>self terminates</td>
</tr>
<tr>
<td><strong>Persistent</strong></td>
<td>&gt;48 hrs and &lt; 6 months</td>
<td>does not self terminate</td>
</tr>
<tr>
<td><strong>Permanent</strong></td>
<td>&gt; 6 months</td>
<td>CV failed or was not attempted</td>
</tr>
</tbody>
</table>

- **First detected** episode should be defined clinically
- **Secondary** e.g. thyrotoxicosis, alcohol
- **Lone** - no clinical or echo evidence of disease
Duration of Atrial Fibrillation Predicts Likelihood of Remaining in Normal Sinus Rhythm after Cardioversion

Dittrich HC. Am J Cardiol. 1989; 63: 193-197
Atrial Fibrillation in Heart Failure: Prognosis

SOLVD Trials Findings
Atrial Fibrillation and Mortality Risk - SOLVD Trials: All Cause Mortality

Mean EF=26% (SR and AF groups)
NYHA class III/IV: 22%-AF, 12%-SR (p=0.001)

SOLVD Investigators, JACC 1998
Atrial Fibrillation and Mortality Risk - SOLVD Trials: Pump Failure Deaths

SOLVD Investigators, JACC 1998

Mean EF=26% (SR and AF groups)
NYHA class III/IV: 22%-AF, 12%-SR (p=0.001)

p<0.001
SOLVD Trials - Implications

- Increased all cause mortality in those with AF versus SR at baseline [34% vs 23%, p<0.001]
- Increased pump failure deaths in AF [16.7% vs 9.4%, p<0.001]
- No difference in SCD between AF and SR groups
- AF group more likely than SR group to reach composite end point of death or CHF hospitalization [45% vs 33%, p<0.001]
- Suggests AF is associated with progression of LV systolic dysfunction
Survival of Patients with and without Atrial Fibrillation

(UCLA data 1996)
Atrial fibrillation is a marker for worse outcomes in heart failure CHARM Olsson et al JACC 2006;47:1997

Time to cardiovascular death or heart failure hospitalization

Cumulative distribution function

Year

Low EF:
Hazard ratio 1.29
(95% CI 1.14-1.46)
p<0.001

AF at baseline (Low EF)
No AF at baseline (Low EF)
LVEF > 0.40

AF at baseline (Preserved)
No AF at baseline (Preserved)
LVEF > 0.40

Preserved EF (PEF):
Hazard ratio 1.72
(95% CI 1.45-2.06)
p<0.001

Number at risk
No AF & Low EF 3906 3207 2755 1963
No AF & PEF 2545 2294 2096 1276
AF & Low EF 670 509 417 289
AF & PEF 478 399 353 203

AF predicted mortality for both preserved EF and depressed EF groups and CV death or heart failure hospitalizations for preserved EF group.
# Prognostic Significance of Atrial Fibrillation in Patients with Congestive Heart Failure

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>NYHA</th>
<th>No. of Patients</th>
<th>Patients in AF</th>
<th>Mean Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Middlekauff*</td>
<td>1991</td>
<td>III-IV</td>
<td>390</td>
<td>75</td>
<td>19</td>
</tr>
<tr>
<td>Bourassa*</td>
<td>1993</td>
<td>II-III</td>
<td>6273</td>
<td>731</td>
<td>12</td>
</tr>
<tr>
<td>Matthew*</td>
<td>2000</td>
<td>I-IV</td>
<td>7788</td>
<td>866</td>
<td>37</td>
</tr>
<tr>
<td>Dries*</td>
<td>1998</td>
<td>II-III</td>
<td>6517</td>
<td>419</td>
<td>30</td>
</tr>
<tr>
<td>Opasich**</td>
<td>1998</td>
<td>I-IV</td>
<td>3327</td>
<td>755</td>
<td>12</td>
</tr>
<tr>
<td>Mahoney**</td>
<td>1999</td>
<td>II-IV</td>
<td>234</td>
<td>62</td>
<td>13</td>
</tr>
<tr>
<td>Crijns**</td>
<td>2000</td>
<td>III-IV</td>
<td>427</td>
<td>84</td>
<td>40</td>
</tr>
<tr>
<td>Carson**</td>
<td>1993</td>
<td>II-III</td>
<td>795</td>
<td>107</td>
<td>24</td>
</tr>
</tbody>
</table>

* Studies suggesting significantly increased mortality associated with atrial fibrillation (AF) in patients with congestive heart failure

** Studies in which atrial fibrillation did not significantly increase mortality

Prognostic Significance of Atrial Fibrillation in Patients with Congestive Heart Failure (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>MORTALITY</th>
<th></th>
<th></th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>SR</td>
<td>AF</td>
<td></td>
</tr>
<tr>
<td>Middlekauff*</td>
<td>32%</td>
<td>29%</td>
<td>48%</td>
<td>0.0013</td>
</tr>
<tr>
<td>Bourassa*</td>
<td>18%</td>
<td>NA</td>
<td>NA</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Matthew*</td>
<td>34%</td>
<td>32%</td>
<td>43%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dries (16)*</td>
<td>27%</td>
<td>23%</td>
<td>34%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Opasich**</td>
<td>16%</td>
<td>NA</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td>Mahoney**</td>
<td>19%</td>
<td>16%</td>
<td>23%</td>
<td>0.21</td>
</tr>
<tr>
<td>Crijns**</td>
<td>50%</td>
<td>47%</td>
<td>60%</td>
<td>0.04</td>
</tr>
<tr>
<td>Carson**</td>
<td>25%</td>
<td>21%</td>
<td>20%</td>
<td>0.18</td>
</tr>
</tbody>
</table>

* Studies suggesting significantly increased mortality associated with atrial fibrillation (AF) in patients with congestive heart failure

** Studies in which atrial fibrillation did not significantly increase mortality

Individuals with AF or CHF who subsequently develop the other condition have a poor prognosis.

Unadjusted Cumulative Incidence of First CHF in Individuals with AF

Unadjusted Cumulative Incidence of First AF in Individuals with CHF

AF and CHF: Cox Multivariate Proportional Hazards Models Examining the Impact of the Comorbid Condition on Mortality

<table>
<thead>
<tr>
<th>Models</th>
<th>Men, Adjusted HR (95% CI)</th>
<th>Women, Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbid condition as a time-dependent variable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(A) Mortality after AF impact of incident CHF</td>
<td>2.7 (1.9 to 3.7)*</td>
<td>3.1 (2.2 to 4.2)*</td>
</tr>
<tr>
<td>(B) Mortality after CHF impact of incident AF</td>
<td>1.6 (1.2 to 2.1)**</td>
<td>2.7 (2.0 to 3.6)*</td>
</tr>
<tr>
<td>Comorbid condition as a categorical variable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(C) Mortality after AF impact of prior CHF</td>
<td>2.2 (1.6 to 3.0)*</td>
<td>1.8 (1.3 to 2.3)*</td>
</tr>
<tr>
<td>Impact of concurrent CHF</td>
<td>2.4 (1.6 to 3.5)*</td>
<td>1.4 (1.0 to 1.9)</td>
</tr>
<tr>
<td>(D) Mortality after CHF impact of prior AF</td>
<td>0.8 (0.6 to 1.0)</td>
<td>1.2 (0.9 to 1.6)</td>
</tr>
<tr>
<td>Impact of concurrent AF</td>
<td>1.0 (0.7 to 1.4)</td>
<td>1.1 (0.8 to 1.5)</td>
</tr>
</tbody>
</table>

* p<0.0001, ** p<0.001

Survival Curves in Heart Failure Patients with AF Who Converted (n=16) and Did Not Convert (n=35) to Sinus Rhythm on Treatment with Amiodarone

From subanalysis of CHF-STAT study

Deedwania, Circulation 1998; 98:2574
AFFIRM: Antiarrhythmic Drug Substudy

- Amiodarone (n=106)
- Class 1 Drugs (n=125)
- Sotalol (n=116)

Percentage without Recurrence vs. Years

(p<0.01)

## Drug use in AF patients

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate-control agents</td>
<td>71.6</td>
<td>56.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Digoxin</td>
<td>64.4</td>
<td>36.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>16.3</td>
<td>22.2</td>
<td>0.09</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>15.8</td>
<td>13.5</td>
<td>0.13</td>
</tr>
<tr>
<td>Sinus-rhythm agents</td>
<td>9.8</td>
<td>12.2</td>
<td>0.88</td>
</tr>
<tr>
<td>Quinidine</td>
<td>5.0</td>
<td>0.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>0.2</td>
<td>6.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antithrombototic agents</td>
<td>35.9</td>
<td>46.4</td>
<td>0.05</td>
</tr>
<tr>
<td>Oral anticoagulants in patients ≥80 years</td>
<td>14.3</td>
<td>47.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anticoagulants in patients with high stroke risk</td>
<td>25.0</td>
<td>46.5</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Kaplan-Meier Cumulative Incidence of the Adjudicated First Recurrence of Atrial Fibrillation or Flutter

Dronaderone (n=828)
Placebo (n=409)

EF=58%
Paroxysmal – 70%
Persistent 30%

Hazard ratio, 0.75 (95% CI, 0.65 to 0.87)
P<0.001
# Drugs for Maintenance of Sinus Rhythm in CHF

<table>
<thead>
<tr>
<th>Class</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Quinidine, Procainamide, Disopyramide</td>
</tr>
<tr>
<td>IC</td>
<td>Flecainide, Propafenone, Moricizine</td>
</tr>
<tr>
<td>III</td>
<td>Sotalol, Amiodarone, Ibutilide, Dofetilide</td>
</tr>
<tr>
<td>II</td>
<td>Beta Blockers</td>
</tr>
<tr>
<td>IV</td>
<td>Calcium Channel Blockers</td>
</tr>
</tbody>
</table>

*Emerging Role: ACE inhibitors, ARBs*

**FDA Approved:** Quinidine, Flecainide, Propafenone, Ibutilide, Sotalol, Dofetilide

**AMIODARONE** is NOT FDA approved for treatment of Atrial Fibrillation
AFFIRM

- 214 centres U.S./Canada
- N = 4060
- Age ≥ 65 years
- ≥ risk factor for TE
- AF >6 hours, <6 months
- 1 AF episode within 12 wk
- No contraindications for W
- Follow-up 3.5 (2-6) years
- HTN 51%, lone AF 26%
- 2033 rhythm control
- 2027 rate control

All-cause death
27% vs 26%
(p = 0.058)

After adjustment for confounders
p = 0.034

AFFIRM Investigators, NEJM, Dec 5th, 2002
AFFIRM Investigators, NEJM 2002; 347:1825-33
Clinical Trials

Trial Summary

Title: Atrial Fibrillation and Congestive Heart Failure (AF-CHF - Presented at AHA 2007)
Year Presented: 2007
Topic(s): Arrhythmias, Heart Failure/Transplant
Writer: Ms. Sabina A. Murphy (view disclosure)

Description
The goal of the trial was to evaluate rhythm control with rate control among patients with heart failure and atrial fibrillation.

Drugs/Procedures Used
Patients were randomized to rhythm control (n = 682) or rate control (n = 694). Rhythm control included use of electrical cardioversion combined with antiarrhythmic drugs, including amiodarone as first line therapy and dofetilide and sotalol if needed, and additional non-pharmacological therapy in resistant patients. Rate control included use of beta-blockers, digoxin or pacemaker and AV node ablation if necessary. Patients were to receive optimal heart failure therapy and anticoagulation.

Principal Findings
At baseline, 31% of patients had NYHA class III or IV heart failure. Mean LVEF was 27%. Atrial fibrillation was paroxysmal in 31% of patients and persistent in 69%. By trial design, rhythm control was predominantly done with amiodarone (82%) with less use of sotalol (18%) and dofetilide (0.4%) in the rhythm control cohort. In the rate control group, beta-blockers were used in 88% of patients and digoxin in 75%. Crossover from rhythm to rate control occurred in 21% of the rhythm group and from rate to rhythm control in 10% of the rate group.

There was no difference in the primary endpoint of cardiovascular death between the groups (26.7% of the rhythm control group vs. 25.2% of the rate control group, hazard ratio [HR] 1.06, 95% CI 0.86-1.30, p = 0.59). There was also no difference in total mortality (31.8% vs. 32.9%, p = 0.73), stroke (2.6% vs. 3.6%, p = 0.32), worsening heart failure (27.6% vs. 30.8%, p = 0.17) or the composite of CV death, stroke, or worsening CHF (42.7% vs. 45.8%, p = 0.20) for rhythm control vs. rate control, respectively. In the rhythm control group, 39% had cardioversion compared with 8% of the rate control group (p = 0.0001). Bradyarrhythmias were more common in the rhythm control group (8.5% vs. 4.9%, p = 0.007).

Interpretation
Among patients with heart failure and atrial fibrillation, use of rhythm control was not associated with differences in cardiovascular mortality compared with rate control through a mean follow-up of 3 years.

Results of the present study are similar to those of the AFFIRM trial, which also showed no impact on mortality with rhythm control compared with rate control for management of atrial fibrillation. Atrial fibrillation has adverse hemodynamic effects, due in part to an excessive ventricular rate, irregularity of ventricular response, and loss of atrial contraction. These adverse hemodynamic effects could potentially have an unduly negative influence in patients with CHF. Conversely, restoring sinus rhythm can improve cardiac output, exercise capacity, and maximal oxygen consumption. Despite these potential benefits with rhythm control, no impact was observed on clinical events, even worsening heart failure.
AF - CHF Trial
NYHA Class II-IV; EF <35%
One episode of AF within last 6 months
(paroxysmal 31%; persistent 69%) mean age 67 yrs; 18% F; mean EF 27%

RHYTHM CONTROL
N = 682

- Amiodarone 82%
- Sotalol 1.8%
- Dofetilide 0.4%
- DC CV 39%
- Bradycardia 8.5%

RATE CONTROL
N = 694

- Beta Blockers 88%
- ± Digoxin 75%
- DC CV 8%
- Bradycardia 4.9%

Mean F/U = 37 months

RESULT: NO difference in Clinical Outcomes with a mean follow-up of 3 years

1^o CV Mortality
RR = 1.06 (0.86-1.30)

2^o Total Mortality
- Stroke 2.6%
- Worsening CHF 27.6%

Beta Blockers 88%
± Digoxin 75%
DC CV 8%
Bradycardia 4.9%

Mean F/U = 37 months

RESULT: NO difference in Clinical Outcomes with a mean follow-up of 3 years

Roy, D. AHA Scientific Sessions, Nov. 2007
Choice of Rate Control vs Rhythm Control should be individualized for each patient

**Rate Control Preferred**
- Minimally symptomatic
- Antiarrhythmic drug intolerance or inefficacy
- Risk of proarrhythmia
- ? Age >65 yrs
- AF likely to recur
- Patient preference

*RATE CONTROL IS NOT an INFERIOR STRATEGY (4 trials)*

Anticoagulate based on risk factors for stroke

**Rhythm Control Preferred**
- Highly symptomatic
- Antiarrhythmic drug is tolerated and is effective
- ?‘Focal’ Afib-RF available
- ? Age <65 yrs *(AFFIRM)*
- CHF patients *(AFFIRM)*
- Patient Preference

OVER 50% OF AF EPISODES ARE ASYMPTOMATIC IN ‘SYMPTOMATIC’ PTS

Anticoagulation still needed if risk factors for stroke present
Incidence of AF during four year F/U in 1577 post MI patients with reduced EF (average 33%) and Sinus Rhythm at baseline (RR=0.45)

Pedersen, Circulation 1999; 100:376-380
Freedom from AF in 374 “SOLVD Trial” Patients randomly assigned to Enalapril or Placebo

Mean EF=27%
NYHA Class II
‘Prevention’: n=251
‘Treatment’: n=123

Use of Enalapril to Maintain Sinus Rhythm after Cardioversion for Long Term Persistent Atrial Fibrillation

**Number at Risk**

<table>
<thead>
<tr>
<th>Combination</th>
<th>70</th>
<th>59</th>
<th>55</th>
<th>52</th>
<th>52</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>75</td>
<td>47</td>
<td>44</td>
<td>43</td>
<td>43</td>
<td>0</td>
</tr>
</tbody>
</table>

Prevention of Atrial Fibrillation With Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers
A Meta-Analysis

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# PREVENTION OF AF WITH ANGIOTENSIN INHIBITION

## Comparison: 04 Effect of treatment based on class of drug

### Outcome: 01 Atrial Fibrillation

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (95%CI Random)</th>
<th>Weight %</th>
<th>RR (95%CI Random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 ACE inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Den Berg</td>
<td>2 / 7</td>
<td>7 / 11</td>
<td></td>
<td>1.7</td>
<td>0.45[0.13,1.57]</td>
</tr>
<tr>
<td>SOLVD</td>
<td>10 / 186</td>
<td>45 / 188</td>
<td></td>
<td>4.8</td>
<td>0.22[0.12,0.43]</td>
</tr>
<tr>
<td>TRACE</td>
<td>22 / 790</td>
<td>42 / 787</td>
<td></td>
<td>6.6</td>
<td>0.52[0.31,0.87]</td>
</tr>
<tr>
<td>Ueng</td>
<td>18 / 70</td>
<td>32 / 75</td>
<td></td>
<td>7.0</td>
<td>0.60[0.37,0.97]</td>
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<tr>
<td>CAPP</td>
<td>117 / 5492</td>
<td>135 / 5493</td>
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<td>11.4</td>
<td>0.87[0.68,1.11]</td>
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<tr>
<td>STOPH2</td>
<td>200 / 2205</td>
<td>357 / 4409</td>
<td></td>
<td>13.0</td>
<td>1.12[0.95,1.32]</td>
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<tr>
<td>GISSI</td>
<td>665 / 8885</td>
<td>721 / 8846</td>
<td></td>
<td>14.0</td>
<td>0.92[0.83,1.02]</td>
</tr>
<tr>
<td>Subtotal(95%CI)</td>
<td>1034 / 17815</td>
<td>1339 / 19809</td>
<td></td>
<td>58.7</td>
<td>0.72[0.56,0.93]</td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=32.58 df=6 p<0.00001
Test for overall effect z=-2.53 p=0.01

| 02 ARB          |               |             |                   |          |                   |
| Madrid         | 9 / 79        | 22 / 75     |                   | 4.3      | 0.39[0.19,0.79]   |
| ValHeFT        | 116 / 2209    | 173 / 2200  |                   | 11.8     | 0.67[0.53,0.84]   |
| Charm          | 179 / 2769    | 216 / 2749  |                   | 12.5     | 0.82[0.68,1.00]   |
| LIFE           | 179 / 4417    | 252 / 4387  |                   | 12.6     | 0.71[0.59,0.85]   |
| Subtotal(95%CI)| 483 / 9474    | 663 / 9411  |                   | 41.3     | 0.71[0.60,0.84]   |

Test for heterogeneity chi-square=5.25 df=3 p=0.15
Test for overall effect z=-4.12 p=0.00004

| Total(95%CI)    | 1517 / 27089  | 2002 / 29220|                   | 100.0    | 0.72[0.60,0.85]   |

Test for heterogeneity chi-square=48.50 df=10 p<0.00001
Test for overall effect z=-3.74 p=0.0002

**RR = 0.72**
A paradigm shift in treatment of atrial fibrillation : from electrical to structural therapy ?

**Atrial Fibrillation Treatment Options: Summary**

**Atrial Fibrillation**

**Rate Control**
- Beta blocker + digoxin
- Ca Channel blocker + digoxin
- AV node ablation + pacer

**Rhythm Control**
- Antiarrhythmic drugs
  - Propafenone
  - Flecainide
  - Sotalol
  - Amiodarone
  - Dofetilide
  - Disopyramide
  - Quinidine
  - Procainamide
- Catheter ablation
  - Pulmonary veins
  - LA linear lesions
  - RA linear lesions
  - Focal lesions
- Atrial defibrillator
- DC or Chemical CV to reestablish SR as needed
- Surgery
  - MAZE Procedure

**Anticoagulation for all patients with risk factors for stroke.**
Atrial Fibrillation in CHF: Treatment Options

**Rate Control**
- Beta blocker + digoxin
- AV node ablation + pacer /CRT

**Rhythm Control**
- Antiarrhythmic drugs
- Catheter ablation
- Pulmonary vein isolation
- LA linear lesions
- Atrial Defibrillator + CRT

**Surgery**
- MAZE Procedure

**Anticoagulation** for all patients with risk factors for stroke.

DC CV to reestablish SR as needed.